Simultaneous spectrophotometric determination of trimethoprim and sulphamethoxazole in pharmaceutical preparations

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The assay of trimethoprim (I) and sulphamethoxazole (II) in commercial formulations requires prior separation of each drug (B.P. 1973). The present communication presents a simple and rapid spectrophotometric assay for each without the need for separation.

Pure samples of I and II were kindly supplied by Burroughs Wellcome & Co. (London). Septrin tablets (Burroughs Wellcome & Co., London) were purchased locally. N-(1-Naphthyl)-ethylenediamine hydrochloride was kindly supplied by E. Merck (Darmstadt). Solutions of trimethoprim (I) and sulphamethoxazole (II) were prepared separately in 0·1 M hydrochloric acid and the ultraviolet absorption spectrum of each was recorded. Whereas the absorption spectra of I and II are not markedly different in 0·1 M hydrochloric acid, they exhibited an isoabsorptive point at 240·5 nm in solution of pH 7·2 (Fig. 1). Thus a zero absorbance value at 240·5 nm results when a solution of I is measured against a solution of II at the same concentration. Standard solutions of I and II separately in the

concentration range of 6 to 14 μg ml^{-1} obey Beer's law at 240·5 and 255 nm respectively.

The absorbance ratio method of Pernarowski et al (1961) was therefore applied to mixtures of the two components. Thus

$$C_I = \frac{Q_o - Q_{II}}{Q_I - Q_{II}} \cdot \frac{A}{a_i} \quad \cdots \quad \cdots \quad \cdots \quad (1)$$

where C_I is the concentration in g litre^{-1} of component I present in the mixture, Q_o is the ratio of the absorbance values of the binary mixture at two different wavelengths one of which is an iso-absorptive point and the other is a wavelength at which one of the drugs absorbs radiant energy most strongly. Q_I and Q_{II} are the absorbance ratio values for component I and II respectively. A and a_i are the absorbance value of the mixture and the absorptivity of the components respectively, both at the isoabsorptive wavelength. An analogous equation was applied to component II. Known mixtures containing different ratios of I and II were prepared in 0·1 M hydrochloric acid. In the case of the formulated product single Septrin tablets were dissolved in 0·1 M hydrochloric acid. In both cases the acidic solution was suitably diluted and adjusted to pH 7·2 with sodium hydroxide. The absorbance values at 240·5 and 255 nm were then measured.

The average values for five determinations of each of Q_I: 255: 240·5 (trimethoprim), Q_{II}: 255: 240·5 (sulphamethoxazole) and a_i were 1·37 ± 0·004, 0·212 ± 0·001 and 47·0 ± 0·5 respectively. The Q values for the unknown mixtures were calculated similarly and the respective absolute values of I and II were estimated from equation 1. Table 1 shows the average recovery of the individual components in the mixture. The level of components I and II in the tablets (Table 2) are in good agreement with the declared amounts and were comparable with the results using the procedure of the B.P. (1973).
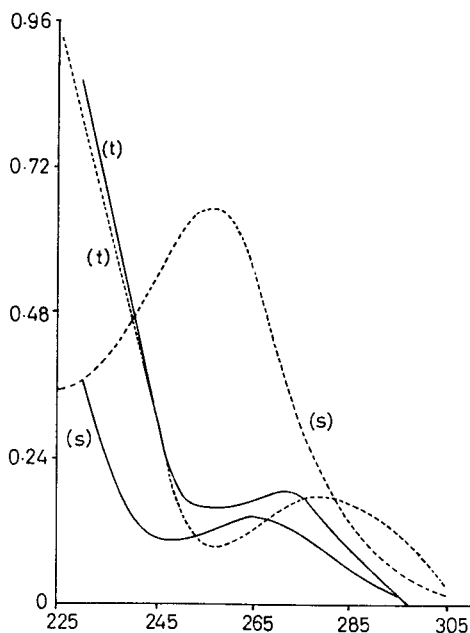

FIG. 1. Ultraviolet absorption spectra of 0·01 g litre^{-1} trimethoprim (t) and sulphamethizole (s) in 0·1 M HCl ——, at pH 7·2 – – –. Ordinate: absorbance. Abscissa: wavelength (nm).

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Table 1. Results of analysis of binary mixtures containing I and II.

Mixture	Concentration of I g litre^{-1} × 10^{-3}		Concentration of II g litre^{-1} × 10^{-3}	
	Present	Found	Present	Found
1	7·00	6·98	7·00	6·95
2	6·00	6·03	8·00	7·94
3	4·20	4·21	9·10	9·07
4	2·34	2·36	11·66	11·67
Average % recovery	100·43 ± 0·65		99·57 ± 0·55	

Table 2. Results of analysis of commercial tablets containing I and II*.

Compound	Present method** average recovery	Present method** % average recovery	B.P. method*** average recovery	B.P. method*** % average recovery
I	80·27 ±3·19	100·34 ±3·97	79·35 ±2·70	99·18 ±3·38
II	398·45 ±6·43	99·61 ±1·61	395·83 ±4·17	98·95 ±1·05

* Septrin tablets containing 80 mg of I and 400 mg of II.
** Average of ten tablets.
*** Average of five tablets.

The advantage of the present method over the official one lies in the simultaneous assay of both I and II without prior separation. This is of value in the study of the dissolution rates of commercial preparations containing I and II, where samples with small volumes are taken at intervals and rapid and accurate assay is required.

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REFERENCE

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Potentiometric analysis with a silver electrode in stability control of quaternary ammonium salt disinfectant solutions during storage in plastic and glass containers

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Several workers have recently reported on the loss of quaternary ammonium compounds from their solutions due to interactions with plastic materials such as plasticized polyvinyl chloride granules, polyethylene and polypropylene which are frequently used for packaging pharmaceuticals (Neuwald & Schmitzek 1968; Quercia et al 1976; Richardson et al 1977). We have recently reported the use of reduced scale potentiometry for the analysis of several quaternary ammonium compounds employing sodium tetraphenylborate solution as titrant and a silver indicating electrode (Pinzauti & La Porta 1977). In the present paper we have extended this work to investigate the possible loss of five different cationic surfactants from 0·1–10% w/v commercially available disinfectant solutions packed in polyolefinic containers. The losses were evaluated by 6 months storage tests at 37 °C and 12 months at room temperature (15–25 °C) and compared with the same solutions in brown glass.

Direct determinations were made either automatically, using a Mettler titrator provided with the essential equilibrium titration control module DK15, or manually by means of a digital pH-meter (Metrohm, E500) and a 5 ml piston microburette calibrated to 0·001 ml (Metrohm, E457). The indicating electrode was a silver spiral 30 cm long. Before each titration the electrode was briefly brought to red heat on a bunsen lamp. It was then soaked for 3 min in a magnetically stirred 3% w/v sodium tetraphenylborate solution previously stabilized (Cooper 1957) and freshly prepared every two weeks, finally it was rinsed with distilled water. This pretreatment replaced that described in our earlier report (Pinzauti & La Porta 1977). When not in use, the electrode was stored in air. The three electrodes employed gave reproducible end point potentials over

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14 months. Potentials were referred to the mercurous sulphate electrode (Metrohm, EA406). An appropriate volume of each disinfectant solution, based on the label claim and corresponding to 8·75–10 mg of surfactant, was transferred into a 50 ml beaker from a 10 ml piston burette calibrated to 0·01 ml, 2 ml of acetate buffer, pH 3·4, were added and the test solution was diluted with water to approximately 20 ml; a 0·01 M sodium tetraphenylborate solution was the titrant. Titration curves, automatically or manually recorded, showed a sharp rise in the potential at the end point (approximately 70 mV per 0·01 ml of titrant operating automatically, and 80 mV per 0·025 ml of titrant operating manually).

Six commercial brands of quaternary ammonium compounds disinfectant solutions, marketed in Italy and freshly prepared, were used (Table 1). Brands A–C were packed in linear polyethylene bottles with polypropylene screw closures, and brands D–F in polypropylene bottles with polypropylene screw closures. Containers of brands A and B were unpigmented, while those of brands C–F contained titanium dioxide. The pH values of commercial solutions ranged from 3·3 to 6·7. Some simulated disinfectant solutions were also prepared, stored in new low density polyethylene (Kartell, Milan, Italy) and glass bottles, and tested for six months at 37°C (0·1 and 15% benzalkonium chloride), or every second day for two weeks at 70°C (0·1% cetylpyridinium chloride, 0·1% benzyldodecylbis-(2-hydroxyethyl)-ammonium chloride, 0·1 and 15% benzalkonium chloride). In the latter case comparative analyses between the potentiometric and spectrophotometric procedures were carried out. The absorbance of aqueous solutions was measured at λ_{max} 269 nm, $\epsilon =$ 1408, for benzyldodecylbis-(2-hydroxyethyl)-ammonium chloride; at λ_{max} 259 nm, $\epsilon = 4920$, for cetylpyridinium chloride; and at λ_{max} 263 nm, $\epsilon = 390$, for